REMARKS

Claims 28-61 are cancelled. Claims 62-70 are added and are now active in this case.

Notably, new independent claim 62 recites:

"comparing, in a third step, the measured effect of said substance, to a previously measured effect in the absence of said substance to determine the relative effect of said substance, and",

The method, thus, defined by claim 62 is directed to a specific methodology for identifying substances which have an effect as defined in step b), upon the activity of Aster Associated Protein (ASAP) or an ortholog as defined within this claim.

Claims 56, 58, 60 and 61 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/070539. However, this document fails to either disclose or suggest the present invention.

WO 02/70539 neither discloses nor suggests the claimed method and it merely follows the work of the present inventors whereby the function of ASAP became known.

Further, even if it is assumed this species of protein is known, the fact this species of protein is associated with the cell cycle would be unknown from this document or from anywhere else in the prior art. The cited document does not provide any information concerning the biochemical or functional properties of this putative ASAP ortholog. The only information provided is that the relevant peptide sequence (1497) comprises a vesicular transport protein SEC17 motif (Table V pg. 613). This would be insufficient information to enable one skilled in the art to put into practice the claimed method. further, WO 02/70539 would provide no motivation for one skilled in the art to even attempt to achieve the claimed invention.

The various methods taught by WO 02/70539 do not relate to the monitoring of the mitotic spindle nor to the measurement of the occurrence of aberrant and abortive mitoses, which are important features applicants have shown to result from inappropriate expression of human or murine ASAP. Instead, the methods disclosed in WO 02/70539 are more general and well known molecular biology methods to detect protein complex formation (pg. 5 1n. 19-24, pg. 6 1n. 1-5), to monitor gene expression levels (pg. 5 1N. 29-35) or to use of fusion proteins (pg. 34 1n 28-34) to further elucidate the function of a candidate protein. In contrast, as noted above the current invention concerns monitoring intracellular mechanisms to determine whether or not a

candidate substance affects these mechanisms.

In conclusion, given that the specific technical features of the claimed method are not disclosed in WO 02/70539, and more generally the function of the ASAP gene is not disclosed in WO 02/70539 and particularly its role in the cell cycle, the method recited in claim 62 is clearly patentable over the cited reference.

This claim is also inventive with respect to WO 02/70539 as no motivation exists for one skilled in the art to select the claimed species of protein in a screening method for substances which affect the cell cycle as outlined above, instead of any one of the other 947 protein molecules disclosed in this document. Clearly, WO 02/70539 would provide no guidance for one skilled in the art to make and use the claimed invention.

Hence, this ground of rejection is unsustainable and should be withdrawn.

Claims 56, 58, 60 and 61 stand rejected under 35 U.S.C. 112, first paragraph, as ostensibly failing to comply with the written description requirement.

Applicants have considered the examiner's comments concerning the species of protein claimed and have introduced a further functional characteristic to define the proteins which applicants seek to protect. In particular, applicants have characterized the proteins as only including ones "wherein intracellular over-expression of said ASAP or an ortholog thereof disturbs the organization of the mitotic spindle".

Applicants have for the first time in this application shown that both the human (SEQ ID NO: 1) and murine (SEQ ID NO: 46) Aster Associated Protein (ASAP) when over-expressed disrupts the mitotic spindle and more generally leads to aberrant mitosis and a cessation of cell division (paragraph 13). In this application, applicants detail the means and provide methods to record such effects and to compare these with ones in which the activity of ASAP may be modified by a further exogenous substance.

Applicants consider this claim to be fully supported by the application as filed, as the species of proteins covered by this claim are defined by both a structural limit with reference to the sequence of human ASAP and a functional limit with reference to their effect upon the mitotic spindle, both limits are clearly defined in the application as filed and means to test whether a species is within such limits are also provide din the current application.

Hence, this ground of rejection is deemed moot.

Claims 56, 58, 60 and 61 stand rejected under 35 U.S.C. 112, second paragraph, as ostensibly being indefinite for "failing to particularly point out and distinctly claim the subject matter" regarded as the invention.

However, in reply the following is noted.

1. Use of 'identity' and 'similarity' in Claim 56

The examiner has requested that applicants amend the term '90% similarity' to '90% identity' in claim 56. Applicants respectfully point out that identity and similarity are different measurements of the relatedness between amino acid or nucleic acid sequences. From the application as filed the terms identity and similarity are defined in paragraphs 33-34 and 36-38 as:

A) **Identity**

The identity of a sequence relative to the sequence of SEQ ID NO: 1 as reference sequence is assessed according to the percentage of amino acid residues that are identical, when the two sequences are aligned, so as to obtain the maximum correspondence between them.

The percentage identity can be calculated by those skilled in the art using a computer program for sequence comparison such as, for example, that of the BLAST series (Altschul et al., NAR, 1997, 25, 3389-3402).

A protein having an amino acid sequence that has at least X% identity with a reference sequence is defined, in the present invention, as a protein whose sequence can include up to 100-X alterations per 100 amino acids of the reference sequence, while at the same time conserving the functional properties of said reference protein. For the purpose of the present invention, the term "alteration" includes consecutive or dispersed deletions, substitutions or insertions of amino acids in the reference sequence.

B) **Similarity**

The similarity of a sequence relative to a reference sequence is assessed according to the percentage of amino acid residues that are identical or that differ by means of conservative substitutions, when the two sequences are aligned so as to obtain the maximum correspondence between them. For the purpose of the present invention, the term "conservative substitution" is intended to mean the substitution of an amino acid with another that has similar chemical or physical properties (size, charge or polarity), which generally does not modify the functional properties of the protein.

A protein having an amino acid sequence that has at least X % similarity with a reference sequence is defined, in the present invention, as a protein whose sequence can include up to 100-X non-conservative alterations per 100 amino acids of the reference sequence. For the purpose of the present invention, the term "non-conservative alterations" includes consecutive or dispersed non-conservative substitutions or insertions of amino acids in the reference sequence.

Given therefore that these terms describe different features of the current invention and that it would be impractical to claim both features using a single measurement, the applicants request this objection to be waived.

2. Modulating

The term "modulating" has been replaced with 'activating or inhibiting' clarifying the type of modulation which the substances identified by the method exhibit. These features come from previous claim 57 and claim 58 which are hereby deleted.

Hence, this ground of rejection is deemed moot.

Formal Matters

Priority Document

A copy of the priority document FR 02/16648 was provided to the International Bureau during the international phase of the parent application and was received on March 22, 2004. Enclosed is a copy of the confirmation from the international bureau confirming their receipt of this priority document.

Minor Amendments to Description

The hyperlinks have been deleted from the application, and a section heading entitled "Brief Description of the Drawings" has been added..

Figure 2

Enclosed is a replacement copy of figure 2, from which the various elements of the electrophoretic gel shown therein may be more readily discerned.

Accordingly, in view of all of the above amendments and remarks, it is urged that this application is now in condition for allowance. Early notice to this effect is earnestly solicited. If any issues remain to be resolved, however, applicants respectfully invite Examiner Mondesi to contact the undersigned.

Applicant hereby petitions for the Commissioner to charge any additional fees or any underpayment of fees which may be required to maintain the pendency of this case or credit any overpayment to Deposit Account No. 04-1061.

Respectfully submitted,

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